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In re Application of:

WAYNE A. BORDER
ERKKI I. RUOSLAHTI

Serial No.: 07/416,656

Filed: October 3, 1989

For: INHIBITING TRANSFORMING
GROWTH FACTOR β TO PREVENT
ACCUMULATION OF EXTRACELLULAR
MATRIXHonorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Group Art Unit: 1800

Examiner: S. Ziska

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Date

By

Theresa A. Brown
Theresa A. Brown, Reg. No. 32,5473/19/92Date of Signature
1.60INFORMATION DISCLOSURE STATEMENT

Sir:

In accordance with 37.C.F.R. § 1.97, enclosed are references relating to the above-identified application, which is a continuation-in-part of U.S. Serial No. 07/415,081, filed September 29, 1989. For the convenience of the Examiner, these references are listed on the attached Form PTO-1449 and a copy of each is enclosed herewith. Also attached is a copy of the Search Report issued in the related PCT Application No. PCT/US90/05566.

The present application is directed to a method treating pathologies characterized by an accumulation of extracellular matrix components by suppressing the activity of TGF β . The claimed invention is also useful for diagnosing such pathologies by determining the level of TGF β in the tissues.

The provided references are relevant for the general disclosure of TGF β , as it relates to extracellular matrix

proteins. However, these references, whether considered individually or in combination, neither anticipate nor render obvious the claimed invention.

WO 88/03151 was cited in the Search Report of the PCT application related to the present application. Page 31, line 15 through page 32, line 8 was specifically cited as the relevant portion of this document. The reference, however, is directed to polypeptides that selectively inhibit or promote thrombin-mediated mitogenesis and not the control of TGF β activity.

Ignotz and Massague (1986) report that TGF β increases the expression of fibronectin and collagen in various cells in culture, and the incorporation of fibronectin and collagen into the extracellular matrix. Ignotz and Massague further report that the anchorage-independent growth of fibroblasts by TGF β can be mimicked with fibronectin and can be blocked by inhibitors of fibronectin binding to the fibronectin receptor.

Roberts et al. (1986) report that injection of TGF β , but not EGF or PDGF, into newborn mice induces angiogenesis and collagen formation. The induction of collagen formation in response to TGF β can be inhibited by antibodies specific for TGF β .

Bassols and Massague (1988) describe the induction of proteoglycan gene expression by TGF β . Bassols and Massague further report that TGF β controls chain elongation and termination during biosynthesis of proteoglycans.

Border et al. (1988) describe the induction of proteoglycans in mesangial cells in response to TGF β , suggesting TGF β may have a role in the production of glomerulonephritis.

Flanders et al. (1988) describe antibodies reactive for TGF β and the use of the antibodies, for example, to detect the presence of TGF β in a sample or to block the binding of TGF β to the TGF β receptor.

MacKay et al. (1989) report the presence of TGF β receptors on glomerular epithelial, endothelial and mesangial cells. MacKay et al. describe effect of TGF β on the proliferation of glomerular cells in cell culture and on the production of collagen and fibronectin by glomerular cells.

Connor et al. (1989) report that the degree of intraocular fibrosis following retinal surgery is correlated to the level of TGF β . The activity was primarily due to TGF β 2, although some activity was also due to TGF β 1.

Chen et al. (1987) describe the stimulatory effect of TGF- β on the synthesis of at least two types of chondroitin sulfate proteoglycans in nonproliferating human arterial smooth muscle cells in culture. The authors also report that TGF- β neither significantly stimulated proliferation of quiescent smooth muscle cells nor inhibited proliferating cells. TGF- β was found not to have a comparable stimulating effect on endothelial cell proteoglycan synthesis as it did on arterial cells.

It is respectfully requested that these references be considered in the examination of this application and that their consideration be made of written record in the application file.

Respectfully submitted,

3/19/92

Date



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